

Listing of Claims

1. (original) An herpes simplex virus wherein the herpes simplex virus genome comprises nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO).

2. (currently amended) The~~An~~ herpes simplex virus according to claim 1 wherein said nucleic acid encodes a mammalian asSCCRO.

3. (currently amended) The~~An~~ herpes simplex virus according to claim 1 wherein said nucleic acid encodes the human asSCCRO.

4. (currently amended) The~~An~~ herpes simplex virus according to claim 1 wherein said nucleic acid encodes a nucleotide sequence having at least 60% sequence identity to the nucleotide sequence complementary to:

- (i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;
- (ii) the mRNA transcript of SEQ ID No.s 1 or 3; or
- (iii) to a fragment of said polynucleotide sequence or mRNA transcript.

5. (currently amended) The~~An~~ herpes simplex virus according to ~~claim 1~~claim 4 wherein said nucleic acid encodes a ~~nucleotide sequence having at least 60% sequence identity to the~~ nucleotide sequence complementary to:

- (i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;
- (ii) the mRNA transcript of SEQ ID No.s 1 or 3; or
- (iii) to a fragment of said polynucleotide sequence or mRNA transcript.

6. (currently amended) The~~An~~ herpes simplex virus according to ~~claim 5~~claim 4 wherein said degree of sequence identity is at least 70%.

7. (currently amended) ~~The~~An herpes simplex virus ~~according to any one of claims~~claim 4
~~to 6~~ wherein a said fragment comprises at least 20 nucleotides and no more than 900 nucleotides.

8. (currently amended) ~~The~~An herpes simplex virus according to claim 1 wherein said
nucleic acid hybridises under high stringency conditions to:

- (i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;
- (ii) the mRNA transcript of SEQ ID No.s 1 or 3; or
- (iii) ~~to a~~ fragment of said polynucleotide sequence or mRNA transcript,
under high stringency conditions.

9. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 8~~ wherein said herpes simplex virus genome further comprises a regulatory sequence
operably linked to said nucleic acid encoding an antisense to the squamous cell carcinoma
related oncogene (as SCCRO), wherein said regulatory sequence has a role in controlling
transcription of said asSCCRO.

10. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 9~~ wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus
genome.

11. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 10~~ wherein said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein
coding sequences of the herpes simplex virus genome.

12. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 11~~ wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2
strain HG52.

13. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 11~~ wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

14. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 13~~ which is a gene specific null mutant.

15. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 14~~ which is an ICP34.5 null mutant.

16. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 13~~ which lacks at least one expressible ICP34.5 gene.

17. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 12~~ which lacks only one expressible ICP34.5 gene.

18. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 17~~ which is non-neurovirulent.

19. (currently amended) ~~The~~An herpes simplex virus ~~as claimed in any one of claims~~claim
~~1 to 18~~ wherein said nucleic acid encoding the asSCCRO forms part of a nucleic acid cassette
integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid
encoding:

- (a) said asSCCRO; and nucleic acid encoding:
- (b) a ribosome binding site; and
- (c) a marker,

wherein the nucleic acid encoding asSCCRO is arranged upstream (5') of the ribosome binding
site and the ribosome binding site is arranged upstream (5') of the marker.

20. (currently amended) ~~The~~An herpes simplex virus according to claim 19 wherein a
regulatory nucleotide sequence is located upstream (5') of the nucleic acid encoding asSCCRO,
wherein the regulatory nucleotide sequence has a role in regulating transcription of said nucleic
acid encoding the asSCCRO.

21. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 19 ~~or 20~~ wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.
22. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims claim 19 to 21~~ wherein a transcription product of the cassette is a bi- or poly- cistronic transcript comprising a first cistron encoding the asSCCRO and a second cistron encoding the marker nucleic acid wherein the ribosome binding site is located between said first and second cistrons.
23. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims claim 19 to 22~~ wherein the ribosome binding site comprises an internal ribosome entry site (IRES).
24. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims claim 19 to 22~~ wherein the marker is a defined nucleotide sequence encoding a polypeptide.
25. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 24 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.
26. (currently amended) The~~An~~ herpes simplex virus ~~according to any one of claims claim 19 to 23~~ wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.
27. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims claim 19 to 26~~ wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3') of the nucleic acid encoding the marker.
28. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 27 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

29. – 32. (cancelled)

33. (currently amended) A method of lysing or killing tumour cells *in vitro* or *in vivo* comprising the step of administering to a patient in need of treatment ~~an~~ the herpes simplex virus ~~as claimed in any one of claims~~ claim 1 to 28.

34. (currently amended) A medicament, pharmaceutical composition or vaccine comprising ~~an~~ the herpes simplex virus ~~as claimed in any one of claims~~ claim 1 to 28.

35. (currently amended) ~~The~~ A medicament, pharmaceutical composition or vaccine as claimed in claim 34 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

36. (currently amended) An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO), wherein (1) the nucleic acid sequence is in at least one of the long repeat regions (R_L), or (2) the herpes simplex virus is non-neurovirulent.

37. – 41. (cancelled)

42. (currently amended) A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment ~~a~~ the herpes simplex virus of claim 36, wherein ~~the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) in at least one of the long repeat regions (R_L).~~

43. (cancelled)

44. (currently amended) The method of claim 42 ~~or 43~~ wherein said herpes simplex ~~viruses~~ virus is capable of killing tumour cells.

45. (currently amended) A method of expressing in vitro or in vivo an antisense to the squamous cell carcinoma related oncogene (asSCCRO), said method comprising the step of infecting at least one cell or tissue of interest with ~~a the~~ the herpes simplex virus of claim 36, wherein ~~the genome of said virus comprises a nucleic acid sequence encoding asSCCRO in at least one of the long repeat regions (R_L), said asSCCRO is~~ operably linked to a transcription regulatory sequence.

46. (cancelled)

47. (original) HSV1716asSCCRO (ECACC accession number 04051901).

48. (original) An herpes simplex virus wherein the herpes simplex virus genome comprises nucleic acid encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide.

49. (currently amended) The~~An~~ herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of a mammalian SCCRO.

50. (currently amended) The~~An~~ herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of human SCCRO.

51. (currently amended) The~~An~~ herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having the sequence of SEQ ID No.5 or the complement thereof.

52. (currently amended) The~~An~~ herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having at least 70% identity to SEQ ID No.5 or the complement thereof.

53. (currently amended) The~~An~~ herpes simplex virus according to claim 52 wherein said degree of sequence identity is at least 80%.

54. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 53~~ wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked to said siRNA, wherein said regulatory sequence has a role in controlling transcription of said siRNA.

55. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 54~~ wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

56. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 55~~ wherein the said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes simplex virus genome.

57. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 56~~ wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

58. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 56~~ wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

59. (currently amended) The~~An~~ herpes simplex virus ~~as claimed in any one of claims~~claim 48 ~~to 58~~ which is a gene specific null mutant.

60. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim
48 to ~~59~~ which is an ICP34.5 null mutant.

61. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim
48 to ~~58~~ which lacks at least one expressible ICP34.5 gene.

62. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim
48 to ~~57~~ which lacks only one expressible ICP34.5 gene.

63. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim
48 to ~~62~~ which is non-neurovirulent.

64. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim
48 to ~~63~~ wherein said nucleic acid encoding said siRNA forms part of a nucleic acid cassette
integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid
encoding :

- (a) said siRNA; and nucleic acid encoding:
- (b) a first regulatory nucleotide sequence; and
- (c) a marker,

wherein the nucleic acid encoding said siRNA is arranged upstream (5') of the first regulatory
nucleotide sequence and the first regulatory nucleotide sequence is arranged upstream (5') of the
marker, wherein said first regulatory sequence has a role in controlling transcription of said
marker.

65. (currently amended) The~~An~~ herpes simplex virus according to claim 64 wherein a
second regulatory nucleotide sequence is located upstream (5') of the nucleic acid encoding said
siRNA, wherein the second regulatory nucleotide sequence has a role in regulating transcription
of said nucleic acid encoding said siRNA.

66. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 64 ~~or 65~~ wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.

67. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim 64 ~~to 66~~ wherein the marker is a defined nucleotide sequence encoding a polypeptide.

68. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 67 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

69. (currently amended) The~~An~~ herpes simplex virus ~~according to any one of claims~~claim 64 ~~to 66~~ wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.

70. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim 64 ~~to 69~~ wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3') of the nucleic acid encoding the marker.

71. (currently amended) The~~An~~ herpes simplex virus as claimed in claim 70 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

72. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim 48 ~~to 71~~ for use in a method of medical treatment.

73. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim 48 ~~to 71~~ for use in the treatment of cancer.

74. (currently amended) The~~An~~ herpes simplex virus as ~~claimed in any one of claims~~claim 48 ~~to 71~~ for use in the oncolytic treatment of a tumour.

75. (cancelled)

76. (currently amended) A method of lysing or killing tumour cells *in vitro* or *in vivo* comprising the step of administering to a patient in need of treatment ~~an~~ the herpes simplex virus ~~as claimed in any one of claims~~ claim 48 to 71.

77. (currently amended) A medicament, pharmaceutical composition or vaccine comprising ~~an~~ the herpes simplex virus ~~as claimed in any one of claims~~ claim 48 to 71.

78. (currently amended) ~~A~~ The medicament, pharmaceutical composition or vaccine as claimed in claim 77 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

79. (currently amended) An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, wherein (a) the siRNA is in at least one of the long repeat regions (R_L), or (b) the herpes simplex virus is non-neurovirulent.

80. – 85. (cancelled)

86. (currently amended) A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein (a) nucleic acid sequence is in at least one of the long repeat regions (R_L), or (b) the herpes simplex virus is non-neurovirulent.

87. (currently amended) The method of claim ~~85 or~~ 86 wherein said herpes simplex virus is capable of killing tumour cells.

88. (original) A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding said siRNA in at least one of the long repeat regions (R_L), wherein said nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.

89. (original) A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with a non-neurovirulent herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding said siRNA, wherein said nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.

90. (new) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 36.

91. (new) The medicament, pharmaceutical composition or vaccine as claimed in claim 90 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

92. (new) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 79.

93. (new) The medicament, pharmaceutical composition or vaccine as claimed in claim 92 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.